TO: TSS/OC

- 1. Date of Obligation: N/A
- 2. Perpose of Project: To support study

Univ. of

3. Progress to Date: Satisfectory

- 4. Expiration Date: N/A
- 5. Project Monitor:

FROM: TSS/CD

Room

A THE PARTY OF THE

THOUGH COURT AND

EMMENTA Subproject

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Project HEAULERA 122

Purpose: To develop a technique for the preparation and characterization of cariffied Heurekinia. This study is closely related to the work of

Initiated: September 1960.

Contractor:

Cost: \$2,000.00

Status: - Unknown.

March 21, 1963

Memorandum tos

Finances

Attached is an accounting of one of the ones they are

waiting for.

Subject:

122-4

Accounting from \$2,000.00 Received from Expenditures: Materials imported drums of 6 and 12 in. 2 Kymographys 2 infusion pump th 6 in drum 1 kyrograph 896.91 1 time maker recon 2. Material purchased Exchange Using an average rate of following were purchased at the approximate \$ value of 325.00 1 Deep freezer 21.00 1 Tonometer of 1 tape record with acessories 120.00 7.00 1 oxigenator for water bath l oven and surgical material and syringes 117.00 64.00 drugs Physiological material: 212.00 Levers, cannules, mercury manometers from IBECC 67.00 l balance (to o.lg) 25.00 Picture rolls 26.00 Paper custer 23.00 Hercury 57.00 Surgical material 32.00 Animals (cots, fowls, rabbits and dogs) 7.09 Food for animals \$2,000.00

March 21, 1963

This is a true statement of expenditures as reported to the fund.

f certify that services or materials have been matingapterly received and the expenditures were incurred on official implices.

Datos 3/27/63

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	(When Filled In)

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182-5

Cost Account 1125. 1089- 1902

Object Class

Date	Remarks and References	Oblizations Incurred	Obligations Liquidated	Unliquidated Balance
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(When Filled In)

122-6: 1

9 Stemptember 1960

MEMORANDUM FOR: COMPTROLLER

ATTENTION : FINANCE DIVISION

SUBJECT : MKULTRA, Subproject 122

Under the authority granted in the memorandum dated 13 April 1953 from the DCI to the DD/A, and the extension of this authority in subsequent memoranda, Subproject 120 has been approved and \$2,000 of the over-all MKULIRA project funds has been obligated to cover the subproject's expenses. This obligation of funds should be charged to Allotmant 1525-1009-1902.

A chief

TSD/Research Branch

APPROVED	FOR OBLIGATION OF FUNDS:
	THE PARTY PA
***************************************	Research Director

1 CERTIFY THAT FUNDS ARE AVAILABLE ORIGINATION REPORTER IN. 15/5
PRAFEE TO ALLOS JAT US. 11055-1109-1176.

AUTHORIZING OFFICER

Date

Distribution:

Orig & 2 - Addressee

1 - 480/00

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1-881

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- If funds, in the form of other than U.S. Dollars were on hand, received, or disbursed during the accounting period, all pertinent data, i.e., rate, method of acquisition, etc., must be shown. If advances have been third parties, enter the total of such advances outstanding at the beginning of the accounting period on line la. made to
- If more space is required to explain receipts, prepare receipt form, number and attach hereto. In every case, completely identify the source of receipts. oi.

The voucher may be

- voucher. When space on form is not sufficient to list all vouchers, prepare a listing on a separate sheer and enter the total under item 3. If advances to third parties are outstanding at the close of the account-When a receipt is not obtained, prepare a certificate and attach as a Attach a voucher for each expenditure and assign a number thereto innumerical sequence. ing period, attach an itemized list and enter the total on line Sa. the receipt obtained from the payee. m
- When accounting not be given for disbursements which are advances to be accounted for. Final credit will not be given for disbursements which are advances to be accoun for advances are obtained, list as expenditures or refund of cash, as appropriate.
- Total receipts entered on the line "Total to Account For" must agree with the total disbursements entered on the line following "Total Accounted For."

W. S. S.

122-10

19 September 1960

MERORANDEM FOR: THE RECORD

VTA

1 TSD/Dudget Officer

SUBJECT

: Manara, Subproject 122, Invoice #1

Allotsent 1125-1009-1902

1. Invotes No. 1 is attached covering the above subproject. Populant abould be made as follows:

Coshier's check in the amount of \$2,000.00

2. The check should be formeded to Chief, TSD/Rassarch Eranch, through tSD/Rassat Officer, no later than Yamay, 3 Colober 1960.

3. This is a final invoice. However, since it is enticicated that redictional finds will be obligated for this project, the files should not be closed.

> Chief TSD/Resporch Brouch

Attached: Involca & Certificatio

Distribution:

GMS & 2 . Altressee

15

Thon Filled In)

I certify that the expenditures listed between and on any streadense were incurred for of itsial purposes of a conflictential netter, that payent or educati thereigh has not been received, and that this accounting is true and correct. 2,000.00 27.022.50 AMOUNT TICSAD VOUCHER NO. (Pinance use only) 71-80 AMOUNT MONEY ORDER See Patenchad Correlationation 11930 TOTAL EXPENSES VOUCHER NO. 7-12 DESCRIPTION X AEF. NO. CLASS CHECK DISBURSEMENTS SIGNATURE OF PAYER SOUE DATE TOTALS TOTAL ACCOUNTED FOR H 5 40 ALLOT. OR COST CASH ON HAND END OF PERIOD SPACE BELOW FOR EXCLUSIVE USE OF FINANCE DIVISION 21 1222 1963 Sicher Cottiio no/mm SIGNATURE OF APPROVING OFFICER SIGNATURE OF CERTIFYING OFFICER 4. REFUNDED HEREWITH CERTIFIED FOR PAYMENT OR CREDIT REGISTANO SA GENERAL ADVANCE CA LEDGER ACCT. NO. YR ACCT. NO. DATE Trivelas PERIOD OF ACCOUNTING 3. VOUCHER APPROYED ٤ 33. 221 022 2,000.00 \$ 2,000.00 P E B . 45-46 L10. Soft appears REVIEWED BY SUBMITTED BY DATE FROM C Advance INCIDES Cab 122 S CONTINE OF AUTHORIZED OFFICER DESCRIPTION DELIGATION REFERENCE NO. CHARGE ALLOTMENT NO. RECEIPTS I CERTIFY FUNDS ARE AVAILABLE TOTAL TO ACCOUNT FOR - ALL OTHER ACCOUNTS :3-39 ACCOUNTING BY INDIVIDUAL FOR ADVANCE Follow Instructions on Reverse 1. CASH ON HAND BEGINNING OF PERIOD ADVANCE ACCOUNTS 13.27 20.02 20.02 -JESCRIPTION ESCRIPTION -PREPARED BY 2. RECEIPT DATE

FORM 282 USE PREVIOUS EDITIONS.

INSTRUCTIONS

- period, all pertinent data, i.e., rate, method of acquisition, etc., must be shown. If advances have been rade to third parties, enter the total of such advances outstanding at the beginning of the accounting period If finds, in the form of other than U.S. Dollars were on hand, received, or disbursed during the accounting
- If more apace is required to explain receipts, prepare receipt form, number and attach hereto. In every case, completely identify the source of receipts. oi
- the receipt obtained from the payee. When a receipt is not obtained, prepare a certificate and attach as a sufficient to list all vouchers, prepare a Listing on a separate sheet voucher. When space on form is not sufficient to list all vouchers, prepare a listing on a separate sheet and enter the total under item 3. If advances to third parties are outstanding at the close of the account-The voucher may be Attach a voucher for each expenditure and assign a number thereto in numerical sequence. ing period, attach an itemized list and enter the total on line Sa. 'n
- When accounting not be given for disbursements which are advances to be accounted for. for advances are obtained, list as expenditures or refund of cash, as appropriate. Final credit will
- Total receipts entered on the line "Total to Account For" must agree with the total disbursements entered on the line following "Total Accounted For."

7-881

182-11

RECEIPT

Receipt is hereby acknowledged of the following check:

Treasurer's Check , dated September 28, 1960.
In the except of \$2,000.00 drawn on the payable to



19 September 1900

ENDORGERM FOR: THE RECORD

VYA

: 200/Bullet Officer

SUBJUCT

: MINIMA, Eubprojeck 122, Invoice fl

Allowent 1125-1009-1902

1. Involce No. 1 is attached occurring the above subproject.
Payant should be ende as follows:

Counter's check in the ecount of \$2,600.00, dress on a local bank, payable to

2. The check should be formuled to Chief, The/Research Extens, through Tay/Religet Officer, no later than Headay, 3 Culture 1500.

3. Twin is a final implies. However, since it is entited in the traditional funds will be chilested for this project, the files should not be closed.

Chler Top/descarch Franch

Atteched:

Involce à Cartifications

Distribution: Origh: 2 - Adimoseo

1 - TSD/FASS

>2 - TSD/RB

TSD (19 Sept. 60)





DEVOICE:

For Services



CERCIFICATIONS

(1) It is hereby certified that this is Invoice No. 1 applying to Cubproject No. 122 of NAMERA, that performence is satisfactory, that services are being ecospitated in accordance with rubund agreements, that a Catalled egenda of the rayments and receipts is on file in TSD/NB, that this bill is just and correct and that payment thereof has not yet been made.

Catef, TSD/Research Branch

Dates

(2) It is hereby certified that this invotes applies to Subproject No. 122 of MODERA which was duly approved, and that the project is being carriedows in accordance with the measurantum of 13 April 1953 from the DCI to the DD/A, and the extension of this authority in subsequent measurands.

Research Director

Date:





9 September 1960

NEMORANDUM FOR: COMPTROLLER

ATTENTION : Finence Division

SUBJECT : MENUGRA, Subproject 122

Under the authority granted in the researches dated 13 April 1953 from the RMI to the BD/A, and the extension of this authority in subsequent researches, Subproject 122 has been approved and \$2,000 of the over-all EMMITTA project funds has been obligated to cover the subproject's expenses. This obligation of funds should be charged to Allotrant 1925-1009-1902.

A Contract of the Contract of

TSD/Research Branch

#FEATURE, TAD	hesearch Director	•
Date	ay and the same an	_

APPROVED FOR OBLIGATION OF FIREDS:

MEMORANDUM FOR: THE RECORD

SURJECT : Project MKULTRA, Subproject 122

1. It is requested that Subaroject 122 be approved to support in part the research project of Univ-

in accordance with the attached proposal.

2. Neurokinin is almost certainly a major mediator in the human "stress" reaction. Its nature and function are not well understood.

Purification and chemical characterization are n necessary preliminary to exploring its biological function.

Less until recently been associated with research program dealing with human stress reactions at Success by in the present study could support materially

project, MKULTRA, Subproject 61.

has been briefed fully on this project.

. This project will be funded through the for security and cover purposes.

The accounting for funds expended shall conform to the catablished procedures of that organization. Title to any permanent equipment shall remain with aniversity in lieu of overhead charges.

 The total cost of this project for a period of one year is estimated to be \$2,000 as indicated in the attached budget. Charges



should be made against Allotment Number 1525-1009-1902. .

 No cleared or witting persons are concerned with the conduct of this project.

forty fulling
TSD/Research Branch

APPROVED FOR OBLIGATION OF FUNDS:

Date 91716

Attachment: Proposal

Distribution: Original Only





122-15

August 15, 1960

MEMORANDUM TO:

SUBJECT: Project Proposal entitled:
Principal Investigator:

This proposal has been circulated to and all comments oppear favorable, parties by those who is a professor of pharmacology at the twould appear from his evaluation that this tesearch could constitute a time scientific contribution. It you may know, has worked with here at a more country refurned to

My only comments are: 1) I do not feel personally able to judge the significance of the research except from a general point of view and, from that standpoint, it opposes to be very invocatent; and 2) my only other reaction is the same as is the robservation for the standard of the same as is the same as in the field of the standard of the standard

Program Director

Enc: 2 copies of Proposal

May 1, 1960.



Dear Sirs:

I have enclosed a proposal for consideration by the substance that eppears to be of great importance in the pathological machanisms by which man's relationship to his environment influences health.

Sincerely yours,



PROPOSAL

Author:
Institution: Department of Pharmacology, University of

The central nervous system evokas, integrates, and modulates the body's adoptive responses to the environment. These responses, necessary to survival when appropriate, are implicated in the etiology and course of disease of many categories when inappropriate. It is well established that reactivity to noxious stimulation can be modulated by the central nervous system through control of the timing and amount of adrenal cortical stimulating hormone (AC TH) from the pituitary gland. Recent experiments at the have shown that another major route for central nervous system modulation of the inflammatory response exists. This latter route is through vasemeter control and through modification of the magnitude of local, neuronal reflexes. A potent vascadilator substance is implicated in these reactions.

The applicant has been one of the hos defined this biochemical substance as neurokinin. Neurokinin apparently is a vasadilator polypeptide formed by the splitting of a protein (globulin) present in extracellula r fluid. This splitting is due to the action of a protectlytic enzyme (neurokinin forming enzyme), possibly an intrancuronal protects. The same enzyme has been observed

in the cerebrospinal fluid and in perfusate of the cerebral ventricle during stimulation of the brain, thus giving a source of the material for study. A crude preparation of powdered neurokinin has been prepared by incubation of globulin with cerebrospinal fluid collected from patients with schizophrenia, which contemplarge amounts of neurokinin-forming enzyme. The application has worked with

e) Immediate Objectives ..

To propore and characterize highly purified neurokinin by chromotographic chamical methods.

f) Long Range Objectives

To define the pharmacologic properties, and contribute to understanding of the physiological and pathological significance of neurokinin.

II. Methods

- a) Obtain neurokinin forming enzyme from human cerebrospinal fluid and from perfusate of cerebral ventricles of laboratory animals during stimulation of the brain.
- b) Proporation of crude neurokinin by Incubation of corebrospinal fluid with globulin, precipitation, and extraction with alcohol.
- c) Aurification of the crude proporation by paper and column chromotographic separation of the components in the crude proparation.
 - d) Pharmacologic studies to identify the active fraction
 - a. Isolated rat uterus, rot duodenum bioassay
 and assay of depressor action on the blood pressure

- e) Pharmacologic reheracterization of the properties of pulific neurokinin.
- Electroencephalographic changes induced by intraventricular and inferenceful injection in the cot.
- Behavioral changes induced by intraventricular injections of neurokinin into unanosthatized cots with implanted intraventricular connulae.
- III. It is expected that these studies will require one year to complete.

Budget

 a) Apparatus to augment equipment available in the

I) Stereotoxic (Horsely Clark) apparetus for perfusion of cerebral ventricles and for placement of intraventricular connulae \$900.00

processes of initiational constants	4.00,00
2) Perfusion pump	200.00
3) Small polyethylene Tubing	50.00
4) Recording kimograph for smooth muscle bloassay	250.00
5) Miscellançous equipment, manemeter, clamps, cannulae	100.00
 b) Drugs and supplies for electrophoresis and for pharmacologic studies 	300.00

c) Animals, animal food, and cages

OTAL \$7,000.00

The author is

The outher is engaged in full time research and teaching. He has worked as a professional for years and has worked specifically with vasodilator polypoptides with the has recently completed a fellowship with the has recently completed a working with neurokinin and becoming acquainted with the point of view of the program.

is a tax exempt organization of the

VI and VII:

This project has not been undertaken previously and no support has been our is being requested of other foundations.

PROPOSAL

Author B/S

The applicant has been one of the investigators who has defined this biochemical substance as neurokinin. Neurokinin apparently is a vasodilator polypeptide formed by the splitting of a protein (globulin) present in extracellular fluid. This splitting is due to the action of a protectivitic enzyme (neurokinin forming enzyme), possibly an intraneuronal protects. The same enzyme has been observed

in the cerebrospinal fluid and in perfusate of the cerebral ventricle during stimulation of the brain, thus giving a source of the material for study. A crude proparation of powdered neurol-kinin has been prepared by incubation of globulin with cerebrospinal fluid collected from patients with schizophrenia, which contains large amounts of neurokinin-forming enzyme. The application has worked with the definition of this agent and in the proparation of crude neurokinin.

e) Immediate Objectives.

To prepare and characterize highly purified neurokinin by chromatographic chemical methods.

f) Long Range Objectives

To define the pharmacologic properties, and contribute to understanding of the physiological and pathological significance of neurokinin.

II. Methods

- o) Obtain neurokinin forming enzyme from human cerebrospinal fluid and from perfusate of cerebral ventricles of laboratory animals during stimulation of the brain.
- b) Proparation of crude neurokinin by incubation of cerebrospinal fluid with globulin, precipitation, and extraction with alcohol.
- c) Aurification of the crude proporation by poper and column chromatographic separation of the components in the crude proporation.
 - d) Phermacologic studies to identify the active fraction
 - a. isolated rat uterus, rat duodenum bioassay
 and assay of depressor action on the blood pressure.

- e) Pharmacologic inharmaterisation of the properties of purific neurokinin.
- 1) Electroencephalographic changes induced by intraventricular and

intercarotid injection in the cat.

IV.

2) Behavioral changes induced by intraventricular injections of

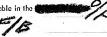
1) Stereotoxic (Horsely Clark) apparatus for perfusion of cerebral

neurokinin into unanesthetized cats with implanted intraventricular connulae.

III. It is expected that these studies will require one year to complete.

Budget

a) Apparatus to augment equipment available in the



ventricles and for placement of intraventricular connulae		\$900.00
7	2) Perfusion pump	200.00
	3) Small polyethylene Tubing	50.00
	4) Recording kimograph for smooth muscle bioassay	250.00
	5) Miscellaneous aquipment, manemeter, clamps, cannulae	100.00
	b) Drugs and supplies for electrophoresis and for	

pharmacologic studies 300.00
c) Animals, animal food, and cages 200.00

imals, animal food, and cages 200.00
TOTAL \$2,000.00

The outlier is

is at tax exempt organization of the State

The author is engaged in full time research and teaching. He has worked as a professional for years and has worked specifically with vasodilator polypeptides with the has recently completed a fellowship with and becoming acquainted with the point of view of the program.

VI and VII:

٧.

This project has not been undertaken previously and no support has been or: is being requested of other foundations.



ATTENDANCE

SUBJECT

Request for \$2000.00 to provide equipment and SUPPARY: supplies for study was approved. Neurokinin is pre-sumed to be a major mediator in the "stress" reaction. Its nature and function are not well understood. Purification and chemical characterization is a necessary preliminary to exploring its biological function. This proposal has received the strong endorse-

> funding mechanism will be the Title to permanent equipment

3. A name check of will remain unwitting of true Sponsor

Research Branch

Distribution: Orig & 3 - Addressee (TSD/RB)



23 August 1960

MEMORANDUM FOR: THE RECORD

SUBJECT

: Discussion with on Proposal

1. At 1100 f bet with Mr

to brief him on the

schanisa, its tripin and its theory technics in participation in the old.

I assured him, in answer to his question, that orrepresents could be used to approach grantees to undertake historias. Further, if his division needed a funding mechanism with sound cover to promote any that could be fitted into the cover, the was available to help out.

2. Although saw no immediate need, he was genuinely enthustastic and wished to make division brass aware of the possibilities.

A VSD/Research Franch

Distribution: Orig & 3 - Addressee (TSD/RB)

for file